



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2009-D-0539]

Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products;

Revised Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised draft guidance for industry entitled “Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products.” This guidance provides recommendations to facilitate industry’s development and validation of immune assays for assessment of the immunogenicity of therapeutic protein products during clinical trials. The guidance for assay development and validation provided in this document applies to assays for detection of anti-drug antibodies (ADA). This document includes guidance regarding the development and validation of screening assays, confirmatory assays, titering assays, and neutralization assays. This guidance revises the draft guidance for industry entitled “Assay Development for Immunogenicity Testing of Therapeutic Proteins” issued in December 2009. This revised draft guidance includes new information on titering and confirmatory assays.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this revised draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the

revised draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2009-D-0539 for “Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products; Revised Draft Guidance for Industry; Availability.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For

more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the revised draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002; or the Office of the Center Director, Guidance and Policy Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5431, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the revised draft guidance document.

FOR FURTHER INFORMATION CONTACT: Ebla Ali Ibrahim, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6308, Silver Spring, MD 20993, 301-796-0281; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7301,

Silver Spring, MD 20993-0002, 240-402-7911; or Peter Hudson, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. G434 (HFZ-410), Silver Spring, MD, 20993-0002, 301-796-6440.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled “Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products.” Patient immune responses to therapeutic protein products have the potential to affect product safety and efficacy. The clinical effects of patient immune responses are highly variable, ranging from no effect at all to extreme harmful effects to patient health. Detection and analysis of ADA formation is a helpful tool in understanding potential patient immune responses. Information on immune responses observed during clinical trials, particularly the incidence of ADA induction and the implications of ADA responses for drug safety and efficacy, is crucial for any therapeutic product development program. Accordingly, such information, if applicable, should be included in the prescribing information as a subsection of the ADVERSE REACTIONS section entitled “Immunogenicity.”

In general, assays for detection of ADA facilitate understanding of the immunogenicity, safety, and efficacy of therapeutic protein products. However, the detection of ADA is dependent on key operating parameters of the assays (e.g., sensitivity, specificity), which vary between assays. Therefore, the development of valid, sensitive, specific, and selective assays to measure ADA responses is a key aspect of therapeutic protein product development.

This guidance revises the draft guidance for industry entitled “Assay Development for Immunogenicity Testing of Therapeutic Proteins” issued in December 2009. The information in

the draft guidance has been reorganized for clarity, and the revised draft guidance includes new information on titering and confirmatory assays.

This revised draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The revised draft guidance, when finalized, will represent the current thinking of FDA on assay development and validation for immunogenicity testing of therapeutic protein products. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This revised draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 314 have been approved under OMB control numbers 0910-0001 and 0910-0230; the collections of information in 21 CFR part 58 have been approved under OMB control number 0910-0119; and the collections of information in 21 CFR part 601 have been approved under OMB control numbers 0910-0338 and 0910-0719.

III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, or <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, or

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>, or <http://www.regulations.gov>.

Dated: April 19, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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